Clinico-pathological conference

Non-tuberculous cavitary disease in a West African man with AIDS

D C W Mabey, S B Lucas, R F Miller

Case Report (*Dr S Lucas*)
The patient was a 34 year old married labourer who lived in Abidjan, the main city of the Ivory Coast in West Africa. He was admitted to hospital with a 4 month history of progressive malaise, anorexia and weight loss of 25 kg. Further questioning on admission to hospital revealed he had persistent fever and intermittent sweats and a non-productive cough. He had not previously sought medical advice for these symptoms and in the past had not previously consulted a doctor or visited hospital. His only risk factor for HIV infection was heterosexual intercourse.

On examination he was cachectic, there was candida in the mouth. The liver and spleen were not palpable and there was no evidence of lymphadenopathy. Investigations included a full blood count which showed him to be profoundly lymphopenic and tests for antibodies to HIV showed him to be HIV 1 antibody positive but HIV 2 antibody negative. A chest radiograph (fig 1) was abnormal showing bilateral mid and upper zone shadowing within which were multiple cavities. Three samples of sputum were obtained, Ziehl-Nielsen staining of these was negative for alcohol and acid fast bacilli (AAFB).

Despite the negative sputum stain there was a high clinical suspicion of tuberculosis and so empirical antituberculous therapy was begun using rifampicin, isoniazid and pyrazinamide in conventional doses. The patient's condition deteriorated rapidly and he died ten days after admission to hospital.

Discussion (*Dr D Mabey*)
We have a 34 year old heterosexual HIV-1 positive Ivoirean man who presents with severe weight loss accompanied by malaise, anorexia, fever and cough. His chest radiograph showed extensive cavitary pneumonia affecting predominantly the upper zones. Although AAFB were not seen in three sputum samples, a strong clinical suspicion of tuberculosis (TB) led to the initiation of antituberculous treatment, but the patient died shortly after admission.

There are many possible causes of cavitary pneumonia in a West African HIV positive male (see table 1), but I agree that TB is by far the most likely diagnosis. It was the commonest cause of adult death in sub-Saharan Africa even before the onset of the AIDS epidemic, and autopsy studies of African AIDS cases have found active TB in at least 25% of cases.[1] A study from Abidjan has shown that 35% of adult tuberculosis is attributable to HIV infection.[2] Next I think we should consider bacterial pneumonia, either with or with-

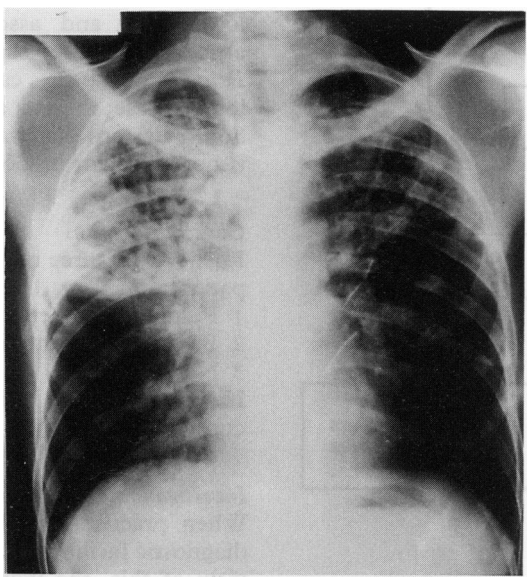

Figure 1 Chest radiograph showing bilateral upper and mid-zone shadowing and consolidation, more marked on the right.

Table 1

Causes of cavitating pneumonia

Common
Mycobacterium tuberculosis
Bacteria
Klebsiella pneumoniae
Staphylococcus aureus
Streptococcus pneumoniae
Pseudomonas aeruginosa
Bacillus/Proteus species
Uncommon
Mycobacterium avium intracellulare
Bacteria
Actinomycosis
Nocardia
Eschericia coli
Serratia/Enterobacter species
Pseudomonas pseudomallei
Rhodococcus equi
Fungi
Histoplasmosis
Coccididioides
Cryptococcus
Pneumocystis carinii
Other
Entamoeba histolytica
Paragonimus westermani
Echinococcus

Department of Pathology
S B Lucas

Department of Medicine, University College and Middlesex School of Medicine, Middlesex Hospital, London, W1N 8AA
R F Miller

London School of Hygiene and Tropical Medicine, London WC1 and Hospital for Tropical Diseases, London, NW1
D C W Mabey

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out underlying TB. Gilks and colleagues have shown that in Nairobi, Kenya septicaemia is common among HIV positive patients, including those without an AIDS defining diagnosis,[3] and the same is likely to be true in other African countries. The organisms most frequently isolated in Nairobi were *Salmonella typhimurium* and *Streptococcus pneumoniae*, but other organisms which are commonly associated with pulmonary abscess, such as *Klebsiella pneumoniae* and *Staphylococcus aureus*, were also isolated. Aspiration pneumonia is unlikely in this patient in view of the predominant upper lobe involvement.

Atypical mycobacterial infections can cause cavitating pulmonary lesions in AIDS patients,[4] and I have seen an ultimately fatal case of cavitating pulmonary disease due to *Mycobacterium avium intracellulare* in an HIV negative Gambian, but it is most unlikely in this case since it is almost never seen in African AIDS cases.[1] Two species of histoplasma cause disease in West Africa: *H capsulatum* and *H duboisii*. The latter usually involves skin, bone and lymph nodes, but pulmonary lesions may occur.[5] Histoplasmosis is a possible diagnosis in this case. Cryptococcus and toxoplasmosis are common in African AIDS, but do not generally cause cavitating pulmonary lesions.

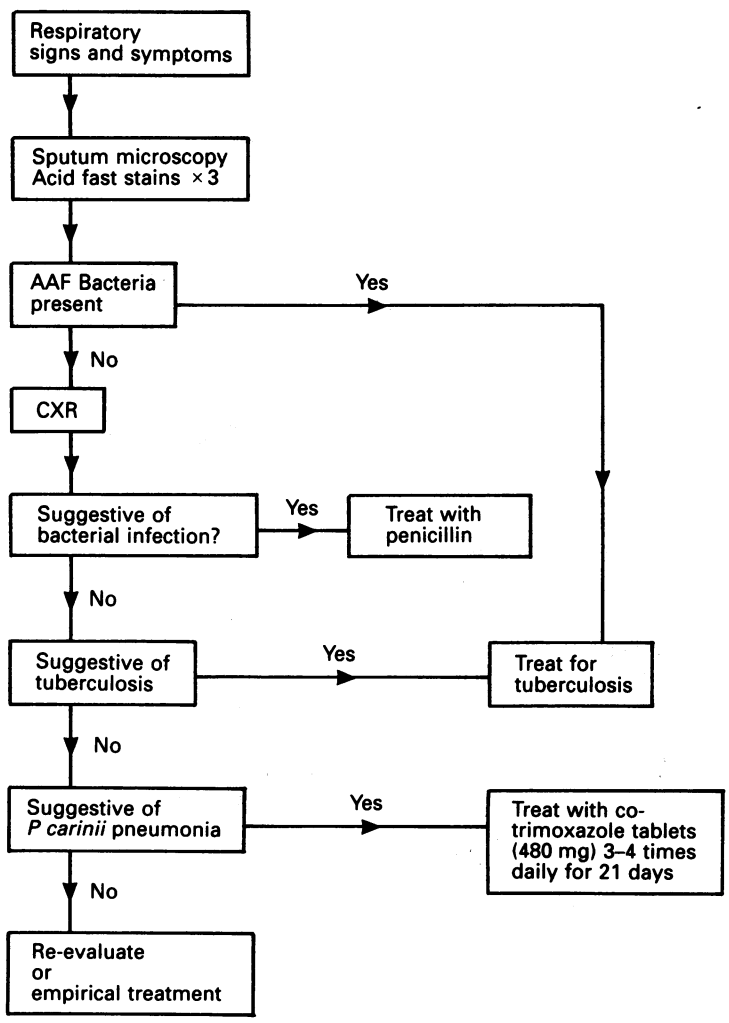
Nocardiosis appears to be more common in Africa than in Europe and America.[6] Nocardiosis was found in three of 57 autopsied AIDS cases in one study in Uganda, and has been reported in Zaire and Cote d'Ivoire.[1] Infection with *Nocardia asteroides*, a saprophytic actinomycete, is well recognised in immunosuppressed patients (particularly recipients of renal and cardiac transplants), in whom it commonly presents with pulmonary or cerebral abscess, but appears to be uncommon in AIDS patients in industrialised countries. Kim and colleagues reported six cases from a New York hospital, comprising 0·3% of all AIDS cases seen, and identified a further eight reported cases.[7] They suggest that the condition may be underdiagnosed because the organism is slow growing; it may be missed unless culture plates are kept for up to four weeks. In another study of 21 cases of pulmonary nocardiosis in HIV positive patients radiographic appearances were varied. Eleven patients (52 %) had lobar or multilobar consolidations, 13 patients (62%) had cavitation and upper lobes were involved in 15 (71%) of patients.[8] It is an important diagnosis to make because it is treatable; the agent of choice is cotrimoxazole, a cheap antimicrobial agent which is widely available in Africa. Nocardiosis should be considered in this patient.

Other rare causes of cavitating pneumonia include melioidosis, caused by the saprophytic bacterium *Pseudomonas pseudomallei*, and *Rhodococcus equi*, a pathogen of horses and cattle which has been reported among AIDS patients in Europe. We have reported a case of melioidosis in West Africa,[9] but I do not know of any other. Both these infections are most unlikely in this case. The incidence of bronchial carcinoma is increasing in many parts of Africa as cigarettes are more widely advertised, but the radiographic appearances in this case do not suggest carcinoma.

Entamoeba histolytica can cause pulmonary abscesses, but these are usually in the right lower lobe and associated with a hepatic abscess; I think we can rule it out in this case. *Paragonimus* species can cause cavitating upper lobe disease; there is a focus of this disease in South Eastern Nigeria, but so far as I know it is not prevalent in Côte d'Ivoire.

Table 2

Investigations



Clinical diagnosis

I believe the three most likely diagnoses in this patient are:

1 Pulmonary tuberculosis
2 Bacterial pneumonia
3 Nocardiosis

He may well have had more than one of these conditions.

Investigation and management of this patient

When practising medicine in Africa optimal diagnostic facilities are not always available. In view of this, the World Health Organisation (WHO) have produced guidelines[10] for the clinical management of HIV infection in adults

Figure 2 Right lung showing upper zone cavitation and widespread pneumoniae with consolidation.

appropriate for use at three levels of health care facility:

Level A: No laboratory or X-ray machine available, eg dispensary or primary health care clinic.

Level B: Microscope and X-ray machine available, eg district hospital.

Level C: Wide range of laboratory and other diagnostic facilities available, eg university teaching hospital.

It appears that the hospital to which this patient was admitted was in category B. The management algorithm suggested for him in the WHO document is shown in table 2. I have to say that I do not agree with this algorithm, which recommends penicillin as the treatment of choice for probable bacterial pneumonia. I would prefer to use co-trimoxazole which is as cheap as oral penicillin, better absorbed and would cover a wide range of possible pathogens including *S aureus*, gram negative bacteria, *P carinii* and *nocardia*. Moreover, in such a sick patient I would want to cover both TB and bacterial pneumonia, since it is clear one will not get a second chance if the initial diagnosis is wrong.

I would also recommend doing a Gram stain of sputum, which can be helpful in diagnosing bacterial pneumonia and nocardiosis. A technique which we have used successfully in Gambian children with pneumonia and pulmonary consolidation is percutaneous needle puncture of the lung, using a 19 gauge needle.[11] I would not recommend it in this case because of the risk of puncturing an apical bulla, but when pulmonary consolidation is present Gram staining of pulmonary aspirate can provide a rapid and reliable diagnosis. It is possible, however, that the risk associated with this procedure may be higher in AIDS patients, due to co-existent autonomic neuropathy.[12]

Autopsy (*Dr S B Lucas*)

Externally the cadaver was of an emaciated middle-aged black male. There was oral candidiasis and no Kaposi's sarcoma. Internally, the oesophagus had candidiasis, and the other organs—with the exception of the lungs—were macroscopically normal.

The apices were adherent to the parietal pleurae. The lungs weighed 925 g (right) and 755 g (left) respectively. The disease was more extensive than the chest radiograph had indicated, with bilateral bronchopneumonia, small foci resembling miliary nodules, and apical cavitation (fig 2). The hilar lymph nodes were unremarkable.

Histology of the lungs showed acute pneumonia and multiple abscesses with intense polymorph infiltration and nuclear karyorrhectic debris. Ziehl-Nielsen stains were negative for acid-fast bacilli, but in the areas of acute inflammation, the Grocott silver stain revealed abundant branching, thin, beaded filaments. These were gram-positive, and weakly acid-fast using a modified Wade-Fite stain: morphologically the bacteria were characteristic of nocardia, although the species could not be identified (fig 3).

The duodenum and jejunum were mildly inflamed and had abundant cryptosporidia adherent to the surface epithelium. No cytomegalovirus infection was found in any tissues;

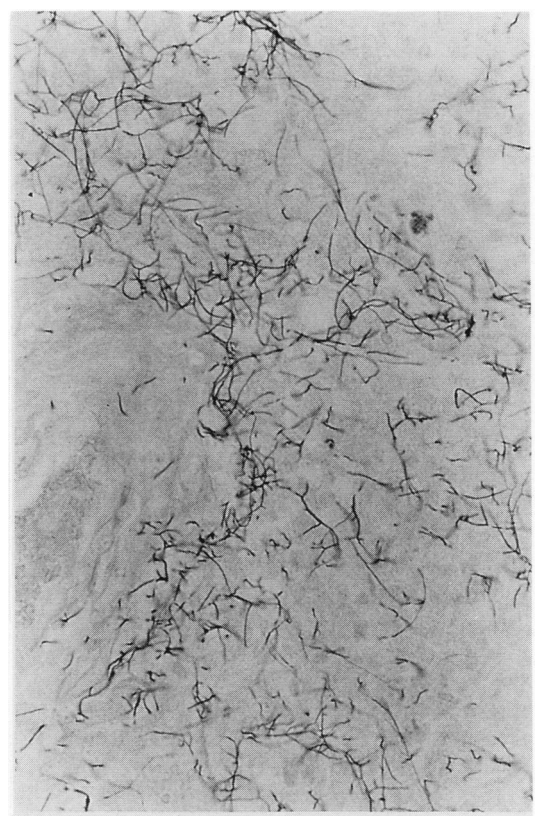


Figure 3 Grocott silver stain showing filamentous, branching nocardia bacilli (× 100).

all lymph nodes showed only atrophy; the brain was normal.

Pathological diagnoses
Oro-oesophageal candidiasis
Severe wasting
Intestinal cryptosporidiosis
Pulmonary nocardiosis
HIV-1 infection

Discussion (*Dr R F Miller*)
We have seen only two cases of pulmonary nocardiosis in our cohort of HIV positive patients. Both patients were profoundly immunosuppressed and had CD4 counts below 100/mm^3. One patient presented with symptoms and signs which were thought initially to be due to *Pneumocystis carinii* pneumonia. The diagnosis of nocardiosis was made by microscopy of bronchoalveolar lavage fluid. The other patient (a recent immigrant from Africa) presented with fever and his chest radiograph showed a focal pneumonia together with hilar and mediastinal lymphadenopathy. The diagnosis was made by microscopy of induced sputum and also from a biopsy of a mediastinal lymph node. Of interest, in both these patients the nocardia infection occurred concurrently with disseminated *Mycobacterium avium intracellulare* infection.

(*Dr S Lucas*)
Although it is not written in the WHO clinical guidelines/management algorithm, one could suggest that in areas where sputum culture for tuberculosis is not practicable, patients with apparent pulmonary tuberculosis who are sputum-negative for AAFB should have further samples stained with Gram's stain to search for nocardia.

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